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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,588	03/29/2002	Ming-Qun Xu	NEB-163-PUS	8694
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NEW ENGLAND BIOLABS, INC. 32 TOZER ROAD BEVERLY, MA 01915			EXAMINER	
			MCKELVEY, TERRY ALAN	
		ART UNIT	PAPER NUMBER	
		1636		
DATE MAILED: 09/30/2003				

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	09/936,588	XU ET AL.
	Examiner Terry A. McKelvey	Art Unit 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 24 July 2003.

2a) This action is FINAL.                    2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 1-25 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) The proposed drawing correction filed on \_\_\_\_\_ is: a) approved b) disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.

12) The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. §§ 119 and 120

13) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All b) Some \* c) None of:

1. Certified copies of the priority documents have been received.
2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

14) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)  The translation of the foreign language provisional application has been received.

15) Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

#### Attachment(s)

1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ .
2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)
3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s) <u>11</u> .	6) <input type="checkbox"/> Other: _____ .

**DETAILED ACTION**

***Priority***

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)). The specific reference to any prior nonprovisional application must include the relationship (i.e., continuation, divisional, or continuation-in-part) between the applications except when the reference is to a prior application of a CPA assigned the same application number.

In the instant case, the first sentence of the application lacks the required priority statement to 60/135,677, which is indicated in the oath/declaration.

***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 1, the use of "A method of reconstituting a target protein in a predetermined location within an organism" followed by the recited steps, ending with "reconstituting the target protein from the protein fragments" renders the claims vague and indefinite because the method steps do not carry out what the preamble states and thus it is unclear what the method comprises. For example, the method steps recite nothing concerning the protein fragments going to or being expressed in a predetermined location. Also, there is nothing in the steps which indicates that the target protein is reconstituted within the organism.

Regarding claim 2, the use of "A method preventing transmission to other organisms of the gene coding for a target protein from within an organism containing said DNA" renders the claims vague and indefinite because it is unclear what is meant by "from within an organism" in the context it is claimed.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 2-9, 12-13, 16-19, and 21 are rejected under 35 U.S.C. 102(b) as being anticipated by Comb et al (U.S. Patent No. 5,496,714).

Comb et al teach: "If a protein is extremely toxic to a host cell it may be desirable to produce that protein using a method referred to as "transsplicing". Using this method the toxic protein is produced in two or more pieces in separate host cells. Each piece being modified by insertion of a CIVPS. For example, a first modified protein can be produced comprising an amino portion of a target protein to which is inserted at its carboxy terminus an amino terminal fragment of a CIVP,

thereafter a second modified protein comprising the remaining portion of the target protein into which is inserted at its amino terminus the remaining fragment of CIVPS. Alternatively, overlapping CIVPS fragments can be used. Each modified protein is then isolated from the host cells and incubated together under appropriate conditions for splicing of the CIVPS. This results in a ligated target protein. By dividing the target protein in two different hosts, there is no possibility that even a minute fraction will splice *in vivo*, adversely affecting the host." (columns 8-9). This reads on the claimed invention because the toxic protein is made by splitting the DNA coding for the (target) protein by intein insertion and separating the DNA fragments into separate host cells (which are different compartments such as different nuclei and which are separated into different DNA such as different DNA from nucleus or vector). This DNA is naturally inherited once in the cell. The protein is reconstituted by intein-mediated splicing/complementation. The division of the target gene inherently results in determining a potential split site before the split is engineered. This reference also teaches that the organism in which the protein can be expressed in can be *E. coli* or other organisms (column 8). The DNA molecule that the DNA

fragments can be inserted into are taught as being any of DNA from a virus, plasmid, etc (column 8).

Claims 1-3, 7-8, 12-13, 18-19, 21, and 25 are rejected under 35 U.S.C. 102(e) as being anticipated by Michnick et al (U.S. Patent No. 6,270,964).

Michnick et al teach protein complementation assays in which a gene encoding protein is split in two to make two genes each encoding a fusion protein consisting of N-terminal or C-terminal part of the protein and a leucine zipper sequence (which acts as an affinity domain) (abstract; columns 3-4). The fusion proteins are coexpressed and reconstituted in the organism, E. coli (abstract). This method reads on reconstituting the protein in a predetermined location within the organism, the cytoplasm, and inherently prevents transmission of the gene to other organisms because the gene is in separated parts. Because the DNA for the gene is in two fragments, they are inserted into two different DNAs such as vector DNAs as taught by the reference, and are naturally inherited in the cells once they are within the cells. The reconstitution of the target protein occurs by affinity domain complementation. The DNA is split by determining a potential split site, looking for a site in the amino acid sequence which

will not disrupt the subdomain (i.e., looking for sequence between folding domains) and splitting the DNA at the site (columns 3-4).

**Conclusion**

No claims are allowed.

Certain papers related to this application may be submitted to Art Unit 1636 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is 703-872-9306. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning rejections or other major issues in this communication or earlier communications from the examiner should be directed to Terry A. McKelvey whose telephone number is (703) 305-7213. The examiner can normally be reached on Monday through Friday, except for Wednesdays, from about 7:30 AM to about 6:00 PM. A phone message left at this number will be

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responded to as soon as possible (i.e., shortly after the examiner returns to his office).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Remy Yucel can be reached on (703) 305-1998.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

*Terry A. McKelvey*

**Terry A. McKelvey, Ph.D.  
Primary Examiner  
Art Unit 1636**

September 28, 2003